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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 12/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,442	NISHIDA ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-9,11 and 16-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *8,9,24,30 and 42* is/are allowed.

6)☒ Claim(s) *1,2,5-7,11,16-23,25-29 and 31-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

NON-FINAL ACTION

The period of suspension is over. After a thorough discussion with a Primary Examiner, Emily Bernhardt, prosecution is re-opened for the following grounds of rejection.

Pending claims are 1, 2, 5-9, 11 and 16-42.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1, 2, 5-7, 11, 16-23, 25-29, 31-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claims 1 and 17 recite the definition of R_1 with indefinite metes and bounds because it appears to have the definition of group A, but it can also be another group that is substituted with "a desired number of substituents of group A". Thus, it is unclear what R_1 can be.

b. Also, in claims 1 and 17, the definition of R_2-R_9 has two provisos with indefinite scope. The first is: "R_6 may also represent two lower alkyl groups in geminal"; however, formula I or I' only allows one R_6. Thus, said proviso is inconsistent with the structure. The second proviso is: "if any one of the substituents R_2-R_9 includes cyclic group, such cyclic group may be substituted by one or two lower alkyl groups". However, many of these rings in the definition of R_2-R_9 may already be substituted with a "methyl group".

Thus, it is unclear if the proviso intends for additional alkyl groups on said rings besides the possible "methyl" group.

c. Claims 5 and 19 recite the definition of R_{6a} and R_{6b} to include "a cyclic amino group ... being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl group, or an N-hydroxyimino group." It does not appear that "N-hydroxyimino group" is a cyclic amino group. Thus, the definition of "a cyclic amino group" is indefinite.

d. Claim 16 lacks antecedent basis because it depends on claim 1, but recites formula VI which is not recited in claim 1.

e. As amended in the amendment of 6-12-02, claim 17 is incomplete for not reciting the structure of formula I".

f. Claim 20 recites the proviso of "if any one of the substituents R_2-R_9 includes cyclic group, such cyclic group may be substituted by one or two lower alkyl groups". The definition of R_2-R_9 has one or two groups having "phenyl" which is open-ended to both unsubstituted or substituted. So, with said proviso, it is not clear if "lower alkyl groups" would be the only possible subsituent(s) on the phenyl ring, or they would be additional substituents on the phenyl ring.

g. Claims 1, 2, 34, 35, 40 and 41 have indeterminate scope because they define disease(s) by its (their) underlying cause renders the scope of the intended uses indeterminate since the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood.

h. Claims 6, 7, 11, 16-23, 25-29, and 31-36 are rejected as being dependent on claim 1, 5, 17, or 20, and carrying over the rejected limitations.

i. Claims 31-33 and 37-39 are substantial duplicates of each other because they recite method of use with no particular steps.

j. **Use Claims:** Claims 31-33 and 37-39 provide for the use of compounds recited in claims 20 and 24, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Use Claims: Claims 31-33 and 37-39 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **Scope of Enablement:** Claims 1, 2, 34, 35, 40 and 41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment or thrombus or embolus, does not reasonably provide enablement for the treatment or prevention of other diseases that are allegedly related to factor Xa (e.g., influenza viral infection, or DIC. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims:

Claim 1 recites: "A method for treating a disease for which the FXa inhibitor is indicated....". Claim 2 depends on claim 1, and thus, carries out the same scope.

Claims 34 and 40 recite: "A method for inhibiting coagulation..."

Claims 35 and 41 recite: "A method for inhibiting activated coagulation factor X..."

All of which includes diseases of thrombotic disorders as well as others such as: DIC (?), and influenza viral infection as cited on page 12 of the specification. Therefore, the scope of said claims are unduly broad in terms of diseases that can be treated.

The amount of direction or guidance presented: While the claimed compounds are shown to inhibit factor Xa in the coagulation cascade, they do not have activity in the treatment of DIC or influenza viral infection. Thus, the specification fails to provides guidance for treating numerous diseases that are allegedly related to factor Xa.

The state of the prior art: Factor Xa inhibitors are well known to treat or prevent blood clot, and are useful in post-op, TIA (transient ischemic attack), or DVT (deep vein thrombosis). However, they are not known to treat influenza viral infection, DIC or anything else. Therefore, the state of the art does not support the scope of the method recited in the above claims.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in undue experimentation to establish data that would adequately support the use of the claimed compounds in the treatment of other diseases related to factor Xa

(e.g, influenza viral infection, DIC, etc.). Such a task would require a tremendous amount of effort, time and resources.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting path ways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification only shows evidence that the claimed compounds can inhibit factor Xa. However, said evidence does not adequately guide the skilled clinician in the treatment of diseases such as influenza viral infecetion or DIC because they have different causative or underlying factors. Thus, with such a limited teaching, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in the methods recited in claims 1, 2, 34, 35, 40 and 41.

Allowable Subject Matter

4. Claims 8, 9, 24, 30 and 42 are allowed.

The following is an examiner's statement of reasons for allowable subject matter:

Claims 8, 9 and 24 recite species, and so do not have indefinite and enablement issues. Claims 30 depends on claim 24, and recites specific pharmaceutical composition, and thus, also free of indefinite and enablement issues. Claim 42 depends on claim 24 and recites specific diseases, and therefore, do not have indefinite and enablement issues. The prior arts of record do not teach or fairly suggest species in claims 8, 9 and 24. The closest prior art, **Tawada et. al.** (US 6,403,595 B1), teaches one species of claim 9,

which is also the species of claim 24. However, said reference does not have a filing date that antedates the instant invention, and thus, it is not a competent prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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November 27, 2005

Tamthom N. Truong
Examiner
Art Unit 1624

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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